Esophageal Cancer Epidemiology in Blacks and Whites: Racial and Gender Disparities in Incidence, Mortality, Survival Rates and Histology

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Background: Esophageal cancer rate disparities are pronounced for blacks and whites. This study presents black–white esophageal cancer incidence, mortality, relative survival rates, histology and trends for two five-year time periods—1991–1995 and 1996–2000—and for the time period 1991–2000.

Methods: The study used data from the National Cancer Institute's population-based Surveillance Epidemiology End Results (SEER) program with submission dates 1991–2000. Age-adjusted incidence, mortality, relative survival rates and histology for esophageal carcinoma were calculated for nine SEER cancer registries for 1991–2000. Rates were analyzed by race and gender for changes over specified time periods.

Results: Esophageal cancer age-adjusted incidence of blacks was about twice that of whites (8.63 vs. 4.39/100,000, $p<0.05$). Age-adjusted mortality for blacks, although showing a declining trend, was nearly twice that of whites (7.79 vs. 3.96, $p<0.05$). Although survival was poor for all groups, it was significantly poorer in blacks than in whites. Squamous cell carcinoma was more commonly diagnosed in blacks and white females, whereas adenocarcinoma was more common among white males ($p<0.001$).

Conclusions: Racial disparities in esophageal cancer incidence, mortality, survival and histology exist. Survival rates from this disease have not significantly improved over the decade. These data support the need for advances in prevention, early detection biomarker research and research on new, more effective treatment modalities for this disease.

Key words: esophageal cancer ■ black–white disparities ■ incidence ■ mortality ■ survival ■ histology

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INTRODUCTION

Although the overall cancer incidence and mortality rates have declined between 1973 and 1998 in the United States,[1] race/ethnic- and gender-based cancer disparities have persisted. African Americans are more likely to develop and die from cancer than any other racial group.[2-6] Black–white disparities in cancer incidence, survival and mortality are evident for most of the common cancers, such as lung, breast, cervix, prostate, colon-rectum and for the less common but lethal esophageal cancer.[6]

Recent trends indicate a dramatic increase in the incidence of esophageal cancer, especially adenocarcinoma of the esophagus, in certain parts of the world, including the United States. Esophageal cancer is relatively common in developing countries of Asia, parts of Europe, Africa (especially in parts of South Africa), Latin America, China, France and Iran.[7] In the United States, esophageal cancer is a lethal disease that accounts for 1% of new cancers and 2.3% of cancer deaths annually. Geographical variations are also observed within the United States, especially among black patients in the coastal areas of South Carolina where rates are notably high.[8]

The demographic (race/ethnic, gender and age), histological and temporal trends for esophageal cancer document increasing incidence of adenocarcinoma for white males.[9,10] Adenocarcinoma of the esophagus, which in the early 1980s accounted for <15% of all esophageal cancers, now represent >60% of all esophageal cancers.[9,11,12] Striking racial/ethnic differences are reported in esophageal cancer histology between white and black patients. Rates of squamous cell carcinoma are higher in blacks than whites, and the reverse is true for adenocarcinoma of the esophagus.[9]

In 2003, approximately 13,900 new cases and 13,000 deaths from esophageal cancer were estimated.[6] For 1996–2000, black males had an age-adjusted incidence rate of 11.4 per 100,000 (vs. 7.5 per 100,000 for white males) and for black females the rate was 4.2 per 100,000 (vs. 2.0 per 100,000 for white females).[4] Moreover, although the lifetime risk of being diagnosed with esophageal cancer among black and white males is similar (i.e., 0.77%), the lifetime risk of dying from the cancer is higher for black males than white males (0.84% vs. 0.71%). Compared with white females, black females had higher lifetime risk of being diagnosed with (0.38% for black females vs. 0.25% for white females) and dying from (0.32% black vs. 0.21% white) esophageal cancer.[4] The five-year relative survival rate (all stages) for esophageal cancer is 13%, with the rate for whites nearly two times higher than that for blacks (15% whites vs. 8% blacks). Blacks in the United States have substantially higher esophageal cancer-related mortality than other racial groups in the United States. For instance, for the period 1996–2000, the age-adjusted esophageal cancer-related mortality rate for black males was 12.2 per 100,000 (vs. 7.3 for white males and 7.5 for males of all races) and 3.4 per 100,000 for black females (vs. 1.7 for white females and 1.8 for females of all races).[4]

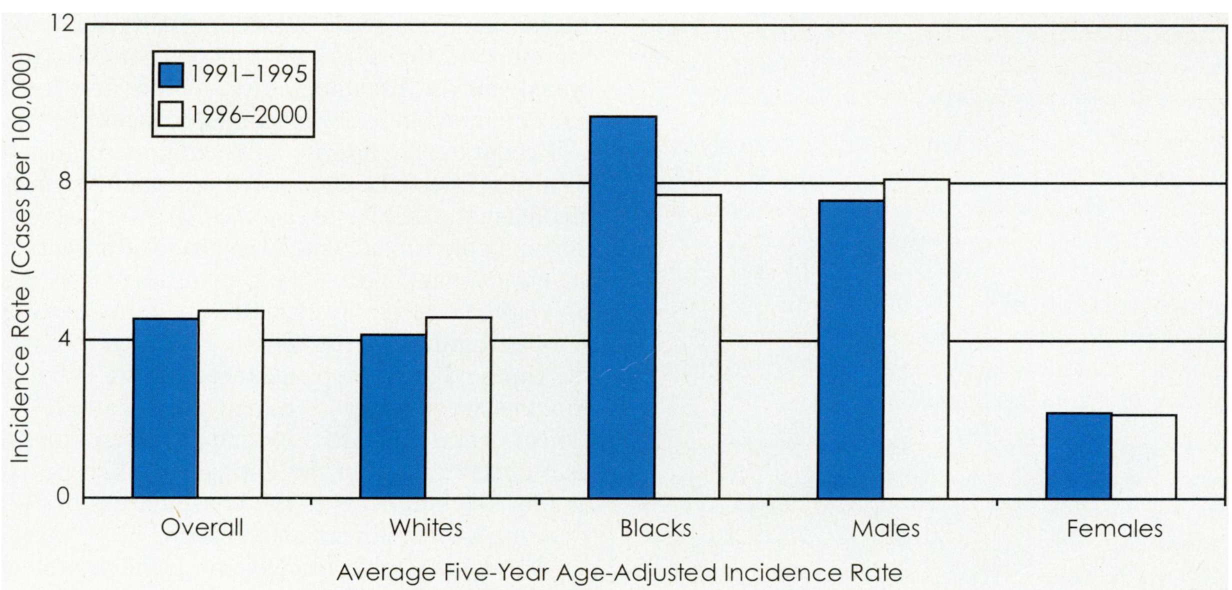
This study provides a comprehensive analysis of esophageal cancer statistics, including age-adjusted incidence and mortality, five-year survival rates and estimated annual percent change (EAPC) for the periods 1991–1995, 1996–2000 and 1991–2000, and cell type for the period 1991–2000. In addition, the report presents race (black–white) and gender disparities for cancer rates and histology. Data presented in this study could form the basis for the development and implementation of esophageal cancer control programs.

METHODS

Incidence, mortality and histology data were obtained from population-based data collected by the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute (NCI).[13] The SEER-9 registry is utilized to obtain statistics for the most recent decade of available data, 1991–2000. Invasive esophageal cancers are included for residents of nine geographical regions comparable to the general U.S. population (in situ cases were excluded). These nine areas are: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco–Oakland, Seattle-Puget Sound and Utah.

The data analysis for this paper was generated using SAS/STAT software (version 8.02) and the NCI SEER software SEER*Stat version 4.2 unless otherwise stated.[14] Age-adjusted incidence and mortality rates for esophageal cancer are expressed per

Figure 1. Esophageal cancer age-adjusted incidence rates: race and gender, 1991–1995 and 1996–2000



Note: Rates are per 100,000 and age-adjusted to the 2000 U.S standard population. Source: Surveillance, Epidemiology and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence—SEER 9 Regs Public-Use, November 2002 Sub (1973-2000), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2003, based on the November 2002 submission.

100,000 population and are age-adjusted by the direct method to the 2000 U.S. standard population.

The incidence data presented in this paper are based on 10,298 invasive esophageal cancers diagnosed between 1991–2000. The racial distribution of these cancers is: 6,369 white males, 2,266 white females, 1,158 black males and 505 black females. Mortality data are based on 106,778 deaths over the 10-year period, and the racial distribution is 88,125 deaths in whites and 18,653 deaths in blacks.

The International Classification of Diseases for Oncology (ICD-O) (2nd edition) codes for histology are used to define esophageal cancer cell types (8000–9581).[15] Cell types are categorized as squamous cell carcinoma (8050–8082), adenocarcinoma (8140–8573) and all other excluding lymphomas (8000–8045, 8090–8130, 8580–9581).[16]

Trend analyses were performed using the EAPC for age-adjusted esophageal cancer incidence and mortality rates and are presented for consecutive five-year periods within 1991–2000 and for the total period. SEER*Stat tests the hypothesis that the EAPC is different from 0 at the 95% level of confidence. Test of equality between the EAPCs for a category over consecutive time periods are based on the method of Kleinbaum.[17]

Rate ratios (the ratio of the two average annual age-adjusted rates) are employed to describe the magnitude of rate disparities between and within race and gender. Rate ratios are tested for statistical significance and trends.[14,17]

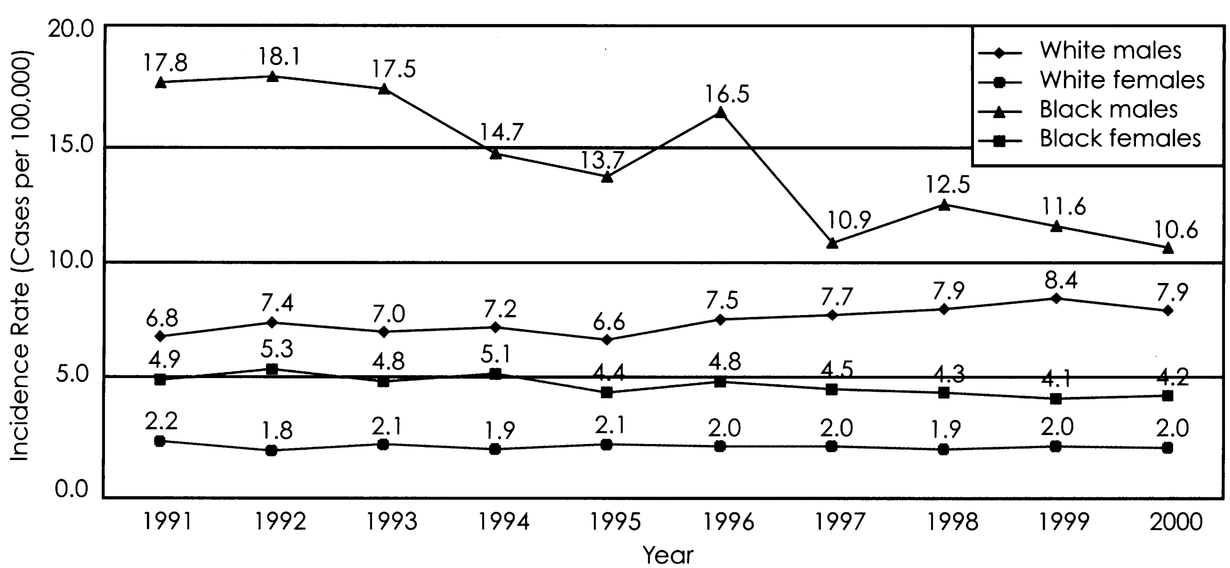
The relative survival rate is a net measure of the influence of esophageal cancer on normal life expectancy in the absence of other causes of death. Since cause of death information on death certificates is often inadequate to determine whether an individual died from the primary cancer diagnosis, the relative survival rate is the preferred method for reporting survival from cancer registry data. Relative survival is the ratio of the proportion of observed survivors in a cancer cohort to the proportion of expected survivors in a comparable cancer-free cohort based on the assumption of independent competing causes of death. The relative survival rate adjusts for the general survival rate of the standard U.S. population for the race, gender, age and date for which the age was coded.[14,18]

RESULTS

Age-Adjusted Incidence

For the period 1991–2000, the overall age-adjusted esophageal cancer incidence rate (IR) was 4.65 (data not shown). Moreover, for the same period, the age-adjusted esophageal cancer incidence rate in blacks was more than twice the rate in whites (8.63 vs. 4.39, $p<0.05$), and males had nearly four times higher incidence (IR=7.84) than females (IR=2.15, $p<0.05$) (data not shown). Age-adjusted incidence rates by race and gender for two consecutive five-year periods—1991–1995 and 1996–2000—are presented in Figure 1. Compared with the age-adjusted incidence rate for the five-year period 1991–1995

Figure 2. Esophageal cancer age-adjusted incidence rates by race and gender, 1991–2000



Note: Rates are per 100,000 and age-adjusted to the 2000 U.S standard population. Source: Surveillance, Epidemiology and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence—SEER 9 Regs Public-Use, November 2002 Sub (1973–2000), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2003, based on the November 2002 submission.

(Figure 1), the age-adjusted incidence rate for the period 1996-2000 was higher overall (4.76 vs. 4.53, $p<0.05$) and also significantly higher for whites (4.60 vs. 4.17, $p<0.05$) and males (8.08 vs. 7.58, $p<0.05$) and lower for blacks (9.69 vs. 7.70, $p<0.05$).

For the period 1991–2000, trends in age-adjusted incidence rates show decreasing rates in blacks (EAPC=-4.81, $p<0.05$) and increasing rates in whites (EAPC=1.68, $p<0.05$) (data not shown). Figure 2 displays age-adjusted incidence rates for the four race-gender groups for individual years 1991–2000. During the period 1991–2000, the trends in age-adjusted incidence rates for black males (EAPC=-5.88, $p<0.05$) and black females (EAPC=-2.47, $p<0.05$) show decreasing rates, whereas, for the same period, the trend for white males (EAPC=2.05, $p<0.05$) shows increasing rates. Although there is a decrease in incidence in blacks, black males continue to have a significantly higher age-adjusted incidence than white males.

When examining rate ratios using the overall average five-year age-adjusted incidence from 1991–2000 (Table 1), blacks have higher incidence than whites overall (RR=1.97, $p<0.05$), and males have substantially higher incidence than females (RR=3.65, $p<0.05$). Blacks of both sexes have incidence ratios higher than whites, and males of both races have rate ratios greater than females, indicating that these groups have significantly higher rates ($p<0.05$). Incidence increased at least 2.5-fold when comparing blacks to whites. The age-adjusted rate ratios differ for time periods 1991–1995 and 1996–2000 by race and for males. Overall, blacks have higher incidence than whites for the time period 1991–1995 when compared with 1996–2000. In addition, black males have higher incidence than white males for the time period 1991–1995 when compared with 1996–2000. White males compared to white females have higher incidence rate ratios for both the five-year time periods.

Age-Adjusted Mortality

For the period 1991–2000, the overall age-adjusted esophageal cancer mortality rate (MR) was 4.27 (data not shown). Moreover, for the same period, the age-

Table 1. Age-adjusted rate ratios (RR) of incidence rates for race and gender over selected time periods

Ratios	1991–2000		1991–1995		1996–2000	
	RR	95% CI	RR	95% CI	RR	95% CI
Blacks to Whites†						
Both genders	1.97	(1.86, 2.07)	2.32‡	(2.15, 2.49)	1.67‡	(1.55, 1.80)
Males	1.90	(1.78, 2.02)	2.34‡	(2.13, 2.54)	1.56‡	(1.42, 1.70)
Females	2.32	(2.09, 2.54)	2.45	(2.11, 2.78)	2.22	(1.92, 2.52)
Males to Females†						
Both races	3.65	(3.49, 3.80)	3.49	(3.28, 3.71)	3.78	(3.55, 4.00)
Blacks	3.08	(2.75, 3.40)	3.33	(2.85, 3.82)	2.82	(2.39, 3.24)
Whites	3.74	(3.56, 3.92)	3.49‡	(3.25, 3.73)	4.01‡	(3.74, 4.27)

† The rate ratios are all significantly different than 1 ($p<0.05$); ‡ The rate ratios differ for time periods 1991–1995 and 1996–2000 (χ^2 statistic, df=1, $p<0.05$); Source: Surveillance, Epidemiology and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence—SEER 9 Regs Public-Use, November 2002 Sub (1973–2000), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2003, based on the November 2002 submission.

Table 2. Age-adjusted rate ratios (RR) of mortality rates for race and gender over selected time periods

Ratios	1991–2000		1991–1995		1996–2000	
	RR	95% CI	RR	95% CI	RR	95% CI
Blacks to Whites†						
Both genders	1.97	(1.94, 2.00)	2.29‡	(2.24, 2.34)	1.70‡	(1.66, 1.74)
Males	1.95	(1.92, 1.99)	2.30‡	(2.24, 2.36)	1.67‡	(1.62, 1.71)
Females	2.25	(2.18, 2.32)	2.51‡	(2.40, 2.62)	2.05‡	(1.96, 2.14)
Males to Females†						
Both races	4.18	(4.12, 4.23)	4.14	(4.06, 4.22)	4.21	(4.13, 4.29)
Blacks	3.76	(3.64, 3.88)	3.92‡	(3.74, 4.10)	3.60‡	(3.43, 3.77)
Whites	4.34	(4.27, 4.41)	4.28‡	(4.19, 4.38)	4.43‡	(4.34, 4.52)

† The rate ratios are all significantly different than 1 ($p<0.05$); ‡ The rate ratios differ for time periods 1991–1995 and 1996–2000 (χ^2 statistic, df=1, $p<0.05$); Source: Surveillance, Epidemiology and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Mortality—All COD, Public-Use With State, Total U.S. (1969–2000), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2003. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).

adjusted mortality rate observed for blacks (MR=7.79) is nearly twice that for whites (MR=3.96, $p<0.05$) and that for males is significantly higher than the rate observed for females (MR=1.80 vs. 7.52 for males, $p<0.05$). For the same period, the age-adjusted mortality rate for black males (MR=13.72) is about twice as high as that observed for white males (MR=7.03, $p<0.05$), and higher age-adjusted mortality rates are also observed for black females compared to white females. Compared with the five-year period 1991–1995, for the period 1996–2000, the age-adjusted mortality rate is higher overall (4.34 vs. 4.21, $p<0.05$), and higher for whites (4.12 vs. 3.79, $p<0.05$) and males (7.62 vs. 7.41, $p<0.05$) and lower for blacks (7.02 vs. 8.68, $p<0.05$). Although a decrease in esophageal cancer mortality is observed among blacks (both males and females), in black males, mortality remains significantly higher than whites.

For the period 1991–2000, trends in age-adjusted mortality rates show decreasing rates overall (EAPC=0.65, $p<0.05$) and in blacks (EAPC=-4.04, $p<0.05$) and increasing rates in whites (EAPC=1.74, $p<0.05$) (data not shown). Age-adjusted mortality rates for the four race-gender groups are presented in Figure 3 for individual years 1991–2000. Between the period 1991–2000, the trends in age-adjusted mortality rates for black males (EAPC=-4.41, $p<0.05$) and black females (EAPC=-3.06, $p<0.05$) show declining rates, whereas, for the same period, the trends for white males (1.78, $p<0.05$) and white females (EAPC=0.87, $p<0.05$) show increasing rates.

Mortality rate ratios are provided in Table 2. Mortality is significantly higher for blacks of both sexes (RR=1.97) than for whites. In addition, males had four-fold greater mortality than females (RR=4.18). Black females have more than twice the mortality of white females.

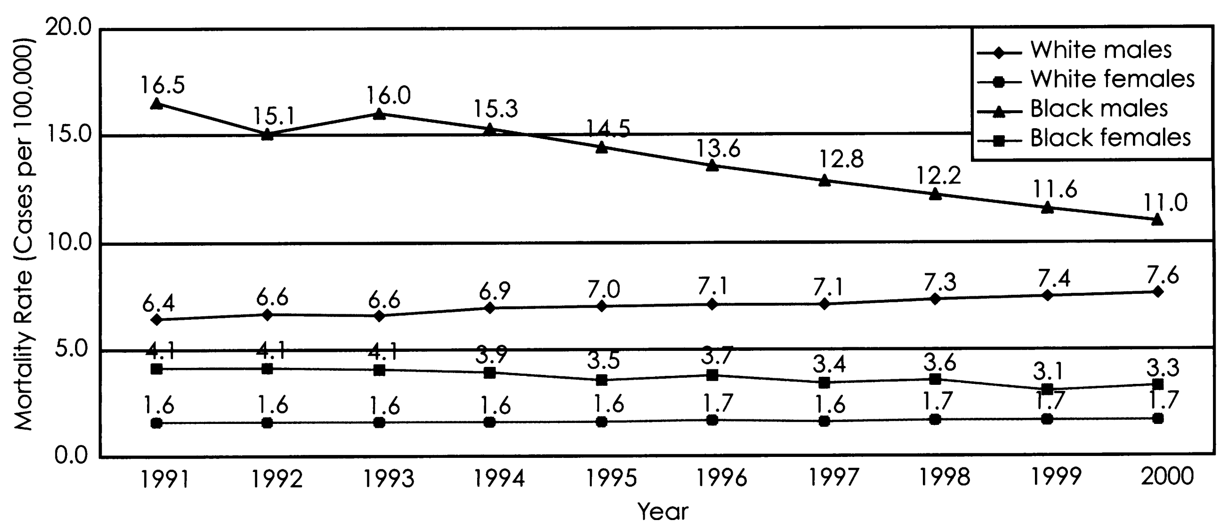
Relative Survival Rates

The overall five-year relative survival rates are poor for both racial groups and for males and females (data not shown). Survival rates of blacks are lower than of whites (6% vs. 12% in whites, $p<0.05$, for period 1991–2000). Few differences are observed in survival rates by gender within each racial group. Black males and females have survival rates (6% for black males and 7% for black females) that are lower than those for white males (11%) and females (12%). Trends in survival from this disease have not significantly improved over the decade.

Histology

Esophageal cancer histology data by race and gender are presented in Table 3, and the age-adjusted incidences by cell type for race and gender for consecutive two-year intervals are displayed in Figure 4. For the period 1991–2000, blacks (males and females) and white females were proportionally more likely to be diagnosed with squamous cell carcinoma than adenocarcinoma (Table 3). During the same time period, white males were more likely to be diagnosed with adenocarcinoma than squamous cell carcinoma (Table 3). Furthermore, the age-adjusted incidence by cell type for race and gender indicates an increasing trend of adenocarcinoma among white males (Figure 4).

Figure 3. Esophageal cancer age-adjusted mortality rates by race and gender, 1991–2000



Note: Rates are per 100,000 and age-adjusted to the 2000 U.S standard population. Source: Surveillance, Epidemiology and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Mortality—All COD, Public-Use With State, Total U.S. (1969–2000), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2003. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).

DISCUSSION

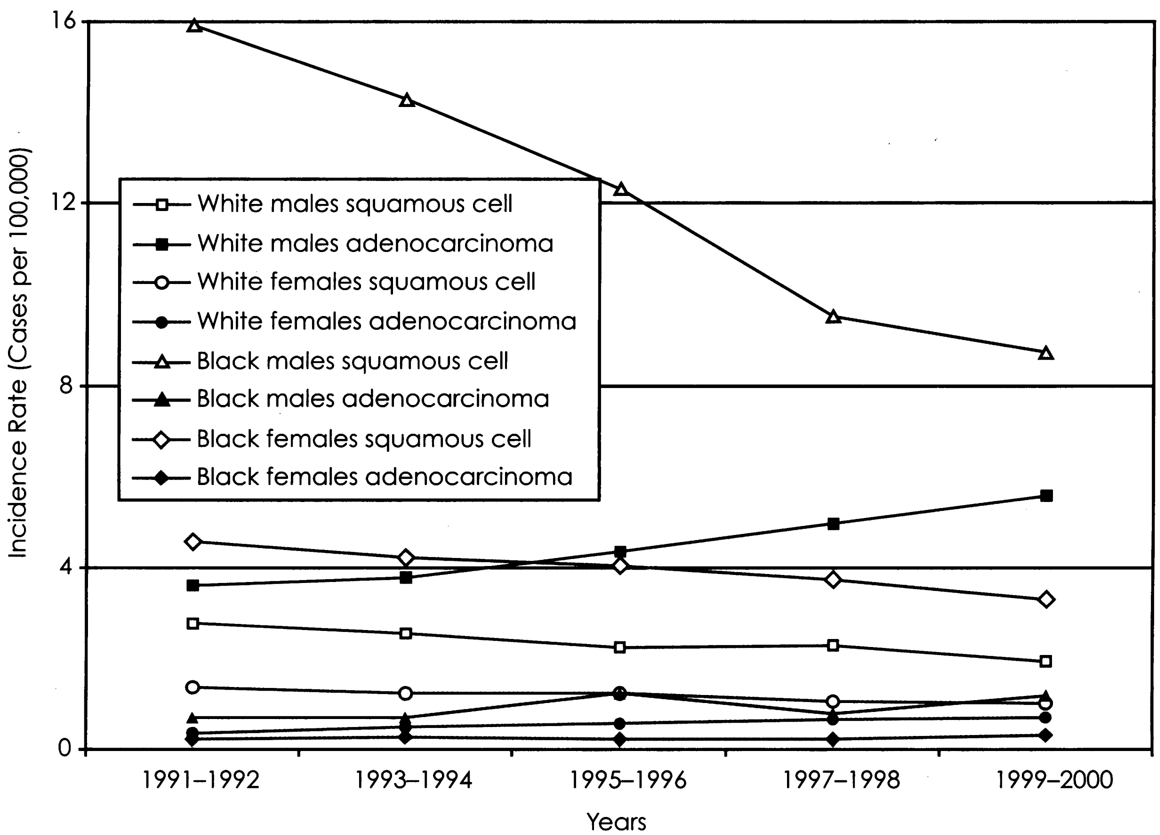
This paper presents detailed esophageal cancer incidence, mortality and relative survival rates for two five-year time periods (1991–1995, 1996–2000) and the entire decade (1991–2000), and histology for the period 1991–2000. Previous studies have reported trends in incidence by race/ethnicity and gender based on SEER data for the period 1974–1994,[9,11] and incidence trends based on SEER data for the period 1973–1998.[10] The results presented in this study indicate that there are persistent age-adjusted disparities in esophageal cancer incidence, mortality and relative survival between blacks and whites, and between black males and females compared with their white counterparts: blacks have higher incidence and mortality rates than whites, and, in addition, blacks have lower relative survival rates than whites. In addition, blacks (males and females) and white females have esophageal squamous cell carcinoma, whereas, white males have esophageal adenocarcinoma.

Table 3. Esophageal cancer histology by race and gender, 1991–2000

Esophageal Cancer Cell Type	Race and Gender				Total
	Black Female	Black Male	White Female	White Male	
Adenocarcinoma	26 (5%)	74 (6%)	643 (28%)	3859 (61%)	4,742
Squamous cell carcinoma	432 (86%)	984 (85%)	1326 (59%)	2000 (31%)	4,602
Other	47 (9%)	100 (9%)	297 (13%)	510 (8%)	954
Total	505	1158	2266	6369	10,298

χ^2 statistic (df=6) for association is statistically significant ($p<0.001$); Source: Surveillance, Epidemiology and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence—SEER 9 Regs Public-Use, November 2002 Sub (1973–2000), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2003, based on the November 2002 submission.

Figure 4. Esophageal cancer age-adjusted incidence by cell type for race by gender for consecutive two-year interval, 1991–2000



Note: Rates are per 100,000 and age-adjusted to the 2000 U.S standard population. Source: Surveillance, Epidemiology and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence—SEER 9 Regs Public-Use, November 2002 Sub (1973–2000), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2003, based on the November 2002 submission.

The risk factors for esophageal cancer are well established and vary dramatically for squamous cell carcinoma and adenocarcinoma. Risk factors for squamous cell carcinoma of the esophagus include diets that are low in fruit and vegetables[9,19,20] or high in meats (red, salted, boiled),[20,21] tobacco use[9,22-25] and alcohol consumption.[9,22,23,25] A synergistic effect is observed among patients who report both tobacco use and alcohol consumption risk factors, especially heavy use. Moreover, consumption of specific alcoholic beverages, such as apple brandies, maize beer, sugar-distilled beverages and moonshine whiskeys, is associated with increased rates of esophageal cancer.[9] The population-attributable risks for ever smoking, alcohol consumption, and low fruit and vegetable consumption have been estimated to account for more than 89% of esophageal squamous cell carcinomas.[26] Other risk factors for squamous cell carcinoma of the esophagus include achalasia,[22] chewing of betel,[24] occupational exposures,[9] ionizing radiation,[9,22] malabsorption disorders,[9,22] history of head and neck cancer,[22] consumption of extremely hot beverages,[9,22,27] genetic abnormalities[9,22,23,28] and familial aggregations.[9] Deficiencies of micronutrients, vitamins and minerals—including iron, beta-carotene, vitamin E, selenium, riboflavin, niacin, retinol, zinc and riboflavin—have also been documented to be associated with increased risk for esophageal cancer, especially in high-risk patients.[9,29] Infection with *Helicobacter pylori* (CagA+) may also increase the risk of squamous cell carcinoma.[30]

The risk factors for adenocarcinoma of the esophagus include Barrett's esophagus;[22,31-35] tobacco use;[9,25] obesity;[9,22,25,36-38] familial aggregation;[9] and genetic abnormalities, such as p53 gene mutation[9] and a history of hiatal hernia, duodenal ulcer, and gastroesophageal reflex disease.[9,35-37] The risk of esophageal adenocarcinoma in patients with Barrett's esophagus is 30–60 times that of the general population.[31] Diets low in fruits and vegetables[9,37] or high in meats[21] and deficiencies of specific micronutrients, vitamins and minerals may also contribute to increased risk for esophageal adenocarcinoma.[9,29] The population-attributable risks for ever smoking, body mass index, history of gastroesophageal reflux, and low fruit and vegetable consumption have been estimated to account for about 79% of esophageal adenocarcinoma.[26] Alcohol use has been inconsistently associated with esophageal adenocarcinoma.[9,25] A protective effect is observed with the use of nonsteroidal anti-inflammatory drugs.[33,39] In addition, infection with *H. pylori* may reduce the risk of adenocarcinoma,[30] although these findings are inconsistent.[40]

There is a paucity of data on the prevalence of esophageal cancer risk factors by race/ethnicity and gender. Although poor diet and nutrition, tobacco use and alcohol consumption are the primary risk factors for squamous cell carcinoma of the esophagus, the prevalence of some of these risk factors may be lower among blacks than whites based on current data.[41] It has been postulated that the higher rates of squamous cell carcinoma of the esophagus in blacks than whites may be due to the differential susceptibility to the carcinogenic effects of alcohol and tobacco.[42,43] The excess prevalence of adenocarcinoma of the esophagus among whites than blacks may be explained by the higher incidence of Barrett's esophagus among whites[34,44] and the general trends of increasing body weight.[45]

The esophageal cancer data presented in this study provides some basis for the need for new basic, clinical and translational research on esophageal cancer. The public health implications are readily apparent based on the relatively higher prevalence of some of the primary risk factors. To the extent that lifestyle and environmental factors, such as tobacco use, alcohol use, poor diet and nutrition, bacterial infection, and obesity, contribute to higher incidence of esophageal cancer, there is a need for targeted public health intervention programs that are guided by advances in basic, clinical, translational and population-based research on esophageal cancer. Public health interventions need to be coupled with new advances in early detection of esophageal cancer.

In conclusion, persistent and new esophageal cancer racial and gender disparities and poor survival rates present an important opportunity for the development of research advances in prevention, early detection and treatment of esophageal squamous cell carcinoma in African Americans and white females and esophageal adenocarcinoma in white males. Because of the high likelihood that this disease will be diagnosed in advanced stages at the time of diagnosis, the opportunity to reduce morbidity and mortality from this disease lies in research advances for the development of new early detection biomarkers and treatment modalities for esophageal squamous cell carcinoma and adenocarcinoma.

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